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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,238	03/29/2004	Kishore K. Wary	D6563	3362

7590 03/17/2008

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
03/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/812,238	WARY ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED _____ FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *8,14,15 and 32*.
   Claim(s) rejected: *None*.
   Claim(s) withdrawn from consideration: *None*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

3/3/2008

/Maher M. Haddad/
Primary Examiner
Art Unit: 1644

Continuation of 11. does NOT place the application in condition for allowance because: 1. Claims 8 and 14-15 stand rejected under 35 U.S.C. 102(b) as being anticipated by Vassilev et al (Blood. 1999 Jun 1 ;93(11):3624-31), as is evidenced by Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) for the same reasons of record.

2. Claims 15 and 32 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,807,819 in view of U.S. Pat. No. 5,567,440 and Vassilev et al as is evidenced by Bendayan (J. Histochem. Cytochem. 1995, 43:881-886) for the same reasons of record.

Applicant's arguments, filed 2/11/08, have been fully considered, but have not been found convincing.

Applicant argues that the instant invention teaches a specific antibody that is directed against a peptide of SEQ ID NO: 41 (5 amino acids) or a peptide of SEQ ID NO: 2 (20 amino acids). Both of these peptides are derived from VCIP of SEQ ID NO: 13 (311 amino acids). The instant antibody was able to block binding of alphavbeta3 and/or alpha5beta1 integrins to the cell surface. Prior to the filing of the instant invention, it was known in the art that alphavbeta3 and alphavbeta5 integrins bind both the proximal RGD site and non-RGD motifs within noncoltagenous domain of the alpha3 chain of Type IV Collagen. In other words, both the RGD and non-RGD motifs contribute to the mechanism of endothelial cell adhesion in the human vasculature (Pedchenko et al., J Biol Chem., 279(4): 2772-2780, 2004). Thus, the instant invention demonstrates for the first time that the RGD motif of VCIP was a potent ligand for a subset of integrins

Contrary to applicant assertion, the claims recite a generic antibody to the claimed peptides of SEQ ID NOs: 2, 13 and 41, wherein the anti-RGD antibody of Vassilev et al would bind to all claimed sequences because they all possess the RGD epitope which the anti-RGD antibody would recognize. It is the Examiner's position that Vassilev et al teachings anticipate the claimed method of inhibiting alphavbeta3 and/or alpha5beta1 integrin ligand-mediated cell-cell interaction with anti-RGD antibodies.

Regarding the 103(a) rejection, Applicant submits that the instant methods use antibodies that are drawn to specific peptides (SEQ ID NOs: 2 and 41) that are either shorter or longer in length than the peptide used by Vassilev et al or different from those taught in US Patent No. 5,807,819 and US Patent No. 5,567,440. Furthermore, the amino acids adjacent to the RGD motif in the peptide of Vassilev et al and US Patent No. 5,807,819 and US Patent No. 5,567,440 are different from the peptides with SEQ ID NOs: 2 and 41. As discussed supra, the evidence provided by Applicants (Lehninger) teach that all the amino acids residues within the antigen are important in determining the specificity of antibody. Therefore, if the peptides or proteins differ in the type of amino acid residues within them, then they will fold differently, which in turn will affect exposure of the specific epitope. Hence, contrary to the Examiner's stand, the conformation of the protein is very important.

However, it is the Examiner's position that the specificity of the antibody is determined by the shared RGD motif among the different peptides, irrespective whether the amino acids adjacent to the RGD motif in the peptide are different in those peptides. The Examiner's position is on line with Applicant's evidence (lehninger) teachings that all the amino acids resiues within the antigen are important in determining the specificity of antibody. Since the antigen in this case is the RGD motif, all three amino acids residures are important in determining the specificity of the antibody, as is evidenced by Vassilev's et al antibody binds different proteins containing the RGD (the antigen). Vassilev et al antibodies meet the claimed limitations that the antibody is directed against a peptie consisting of SEQ ID NOs. 2 or 41, in the absence of evidence to the contrary..